

### Amendments to the Claims

1. (Currently amended) A method for modulating the transport of leptin across the blood-brain barrier of a mammal, the method comprising:

i) administering to the mammal an effective amount of exogenous leptin effective to modulate the transport of leptin across the blood brain barrier; and,

ii) administering to the mammal an effective amount of epinephrine ~~an adrenergic agonist~~ and metabolites thereof,

wherein said administering of step (ii) is effective to modulate the transport of leptin across the blood brain barrier through the specific leptin transporter of the blood brain barrier.

2. (Previously presented) The method of claim 1 wherein said one or more compositions is administered to the mammal via a route of administration selected from the group consisting of intravenous, intraarterial, intramuscular, intraperitoneal, subcutaneous, topical, intraocular, intradermal, transdermal, nasal, oral and pulmonary.

3. (Currently amended) The method of claim 1 wherein the leptin is selected from the group consisting of leptins comprising the amino acid sequence set out as SEQ ID NO: 4, SEQ ID NO: 6, consensus leptins, fragments of leptin set out in SEQ ID NO: 6 selected from the group consisting of residues 98-146, 1-32, 40-116, 1-99 connected to 112-146, and 1-99 connected to 112-146 and having one or more of amino acids 100-111 placed between amino acids 99 and 112, leptin or fragments thereof as set out above having an amino acid substitution at one or more amino acid residues in SEQ ID NO: 6 selected from the group consisting of position 4, 8, 32, 33, 35, 48, 50, 53, 60, 64, 66, 67, 68, 71, 74, 77, 78, 89, 97, 100, 101, 102, 105, 106, 107, 108, 111, 112, 118, 136, 138, 142, and 145, leptin fusion proteins of said leptins, chemically modified derivatives of said leptins of leptin, and fragments thereof, said leptin said leptins optionally having an N-terminal methionine, wherein the leptin is biologically active, and further wherein the leptin retains the ability to be transported across the blood-brain barrier.

4. (Currently amended) The method of claim 2 wherein the leptin is selected from the group consisting of leptins comprising the amino acid sequence set out as SEQ ID NO: 4, SEQ ID NO: 6, consensus leptins, fragments of leptin set out in SEQ ID NO: 6 selected from the group consisting of residues 98-146, 1-32, 40-116, 1-99 connected to 112-146, and 1-99

connected to 112-146 and having one or more of amino acids 100-111 placed between amino acids 99 and 112, leptin or fragments thereof as set out above having an amino acid substitution at one or more amino acid residues in SEQ ID NO: 6 selected from the group consisting of position 4, 8, 32, 33, 35, 48, 50, 53, 60, 64, 66, 67, 68, 71, 74, 77, 78, 89, 97, 100, 101, 102, 105, 106, 107, 108, 111, 112, 118, 136, 138, 142, and 145, leptin fusion proteins of said leptins, chemically modified derivatives of said leptins of leptin, and fragments thereof, said leptin said leptins optionally having an N-terminal methionine, wherein the leptin is biologically active, and further wherein the leptin retains the ability to be transported across the blood-brain barrier.

5. (Currently amended)      The method of claim 1 ~~77~~ wherein the adrenergic agonist is epinephrine.

6. (Withdrawn)      The method of claim 1, 2, 3, or 4 wherein the one or more adrenergic antagonists are selected from the group consisting of yohimbine, phentolamine, prazosin, and benoxathian.

7. (Withdrawn)      The method of any one of claims 1, 2, 3, or 4 wherein the cytokine is TNF- $\alpha$ .

8. (Withdrawn)      The method of claim 1, 2, 3, or 4 wherein the amino acid is tyrosine.

9. (Withdrawn)      The method of claim 1, 2, 3, or 4 wherein the purinergic agonist is adenosine.

10. (Withdrawn)      The method of claim 1, 2, 3, or 4 wherein the glutaminergic agonist is glutamate.

11. (Withdrawn)      A method for modulating body weight in a mammal, the method comprising:

administering to the mammal an effective amount of one or more compositions selected from the group consisting of adrenergic agonists, adrenergic antagonists, neurotransmitters, cytokines, amino acids, opiate peptides, purinergic agonists, glutaminergic agonist, and metabolites thereof.

12. (Withdrawn) The method of claim 11 wherein said one or more compositions is administered to the mammal via a route of administration selected from the group consisting of intravenous, intraarterial, intramuscular, intraperitoneal, subcutaneous, topical, intraocular, intracerebroventricular, intracisternal, intrathecal, intradermal, topical transdermal, nasal, oral and pulmonary.

13. (Withdrawn) The method of claim 11 further comprising co-administering to the mammal of a leptin selected from the group of leptins comprising the amino acid sequence set out as SEQ ID NO. 2, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragments thereof, said leptin optionally having an N-terminal methionine.

14. (Withdrawn) The method of claim 12 further comprising co-administering to the mammal a leptin selected from the group of leptins comprising the amino acid sequence set out as SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragments thereof, said leptin optionally having an N-terminal methionine.

15. (Withdrawn) The method of claim 11 wherein modulating body weight is decreasing body weight.

16. (Withdrawn) The method of claims 11, 12, 13, 14, or 15 wherein the one or more adrenergic agonists are selected from the group consisting of epinephrine, isoproterenol, arterenol, and cirazoline.

17. (Withdrawn) The method of claims 11, 12, 13, 14, or 15 wherein the amino acid is tyrosine.

18. (Withdrawn) The method of claims 11, 12, 13, or 14 wherein the cytokine is TNF-\*.

19. (Withdrawn) The method of claim 11 wherein modulating body weight is increasing body weight.

20. (Withdrawn) The method of claims 11, 12, or 19 wherein the one or more adrenergic antagonists are selected from the group consisting of yohimbine, phentolamine, prazosin, and benoxathian.

21. (Withdrawn) The method of claim 11, 12, or 19 wherein the purinergic agonist is adenosine.

22. (Withdrawn) The method of claim 11, 12, or 19 wherein the glutaminergic agonist is glutamate.

23. (Withdrawn) A method for modulating appetite in a mammal, the method comprising:

administering to the mammal an effective amount of one or more compositions selected from the group consisting of adrenergic agonists, adrenergic antagonists, neurotransmitters, cytokines, amino acids, opiate peptides, purinergic agonists, glutaminergic agonists, and metabolites thereof.

24. (Withdrawn) The method of claim 23 wherein said one or more compositions is administered to the mammal via a route of administration selected from the group consisting of intravenous, intraarterial, intramuscular, intraperitoneal, subcutaneous, topical, intraocular, intracerebroventricular, intracisternal, intrathecal, intradermal, topical, transdermal, subcutaneous, nasal, oral, and pulmonary.

25. (Withdrawn) The method of claim 23 further comprising co-administering to the mammal a leptin selected from the group of leptins comprising the amino acid sequence set out as SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragments thereof, said leptin optionally having an N-terminal methionine.

26. (Withdrawn) The method of claim 24 further comprising the co-administering to the mammal a leptin selected from the group of leptins comprising the amino acid sequence set out as SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragments thereof, said leptins optionally having an N-terminal methionine.

27. (Withdrawn) The method of claims 23, 24, 25, or 26 wherein the one or more adrenergic agonists are selected from the group consisting of epinephrine, isoproterenol, arterenol, and cirazoline.

28. (Withdrawn) The method of claims 23, 24, 25, or 26 wherein the one or more adrenergic antagonists are selected from the group consisting of yohimbine, phentolamine, prazosin, and benoxathian.

29. (Withdrawn) The method of claims 23, 24, 25, or 26 wherein the cytokine is TNF- $\alpha$ .

30. (Withdrawn) The method of claims 23, 24, 25, or 26 wherein the amino acid is tyrosine.

31. (Withdrawn) The method of claims 23, 24, 25, or 26 wherein said purinergic agonist is adenosine.

32. (Withdrawn) The method of claims 23, 24, 25, or 26 wherein the glutaminergic agonist is glutamate.

33. (Withdrawn) A pharmaceutical composition useful for modulating body weight, the composition comprising a leptin selected from the group of leptins comprising the amino acid sequence set out in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragments thereof, said leptin optionally having an N-terminal methionine, in combination with an effective amount of an andrenergic agonist, adrenergic antagonist, neurotransmitter, cytokine, amino acid, opiate peptide, purinergic agonist, glutaminergic agonist, and metabolites thereof.

34. (Withdrawn) The pharmaceutical composition of claim 33 wherein the one or more adrenergic agonists are selected from the group consisting of epinephrine, isoproterenol, arterenol, and cirazoline.

35. (Withdrawn) The pharmaceutical composition of claim 33 wherein the one or more adrenergic antagonists are selected from the group consisting of yohimbine, phentolamine, prazosin, and benoxathian.

36. (Withdrawn) The pharmaceutical composition of claim 33 wherein the cytokine is TNF- $\alpha$ .

37. (Withdrawn) The pharmaceutical composition of claim 33 wherein the amino acid is tyrosine.

38. (Withdrawn) The pharmaceutical composition of claim 33 wherein said purinergic agonist is adenosine.

39. (Withdrawn) The pharmaceutical composition of claim 33 wherein the glutaminergic agonist is glutamate.

40. (Withdrawn) The use of one or more adrenergic agonists or metabolites thereof for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.

41. (Withdrawn) The use of claim 40 wherein the one or more adrenergic agonists are selected from the group consisting of epinephrine, isoproterenol, arterenol, and cirazoline.

42. (Withdrawn) The use of one or more adrenergic antagonists or metabolites thereof for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.

43. (Withdrawn) The use of claim 42 wherein the one or more adrenergic antagonists are selected from the group consisting of yohimbine, phentolamine, prazosin, and benoxathian.

44. (Withdrawn) The use of one or more neurotransmitters or metabolites thereof for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.

45. (Withdrawn) The use of one or more peptide hormones for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.

46. (Withdrawn) The use of one or more cytokines for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.

47. (Withdrawn) The use of claim 46 wherein the cytokine is TNF- $\alpha$ .
48. (Withdrawn) The use of one or more amino acids for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.
49. (Withdrawn) The use of claim 48 wherein the amino acid is tyrosine.
50. (Withdrawn) The use of one or more opiate peptides for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.
51. (Withdrawn) The use of one or more purinergic agonists for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.
52. (Withdrawn) The use of claim 51 wherein said purinergic agonist is adenosine.
53. (Withdrawn) The use of a glutaminergic agonist for the manufacture of a medicament for modulating the transport of leptin across the blood-brain barrier.
54. (Withdrawn) The use of claim 53 wherein the glutaminergic agonist is glutamate.
55. (Withdrawn) The uses according to any one of claims 38 to 54 further comprising the use of leptin for the manufacture of said medicament for modulating the transport of leptin across the blood-brain barrier.
56. (Withdrawn) The use according to claim 55 wherein said leptin is selected from the group consisting of leptin comprising the amino acid sequence set out as SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragment thereof, said leptin optionally having an N-terminal methionine.
57. (Withdrawn) The use of one or more adrenergic agonists or metabolites thereof for the manufacture of a medicament for modulating the body weight of a mammal.
58. (Withdrawn) The use of claim 55 wherein the one or more adrenergic agonists are selected from the group consisting of epinephrine, isoproterenol, arterenol, and cirazoline.

59. (Withdrawn) The use of one or more adrenergic antagonist or metabolites thereof for the manufacture of a medicament for modulating the body weight of a mammal.

60. (Withdrawn) The use of claim 59 wherein the one or more adrenergic antagonists are selected from the group consisting of yohimbine, phentolamine, prazosin, and benoxthian.

61. (Withdrawn) The use of one or more neurotransmitters or metabolites thereof for the manufacture of a medicament for modulating the body weight of a mammal.

62. v (Withdrawn) The use of one or more peptide hormones for the manufacture of a medicament for modulating the body weight of a mammal.

63. (Withdrawn) The use of one or more cytokines for the manufacture of a medicament for modulating the body weight of a mammal.

64. (Withdrawn) The use of claim 63 wherein the cytokine is TNF.

65. (Withdrawn) The use of one or more amino acids for the manufacture of a medicament for modulating the body weight of a mammal.

66. (Withdrawn) The use of claim 65 wherein the amino acid is tyrosine.

67. (Withdrawn) The use of one or more opiate peptides for the manufacture of a medicament for modulating the body weight of a mammal.

68. (Withdrawn) The use of one or more purinergic agonists for the manufacture of a medicament for modulating the body weight of a mammal.

69. (Withdrawn) The use of claim 68 wherein said purinergic agonist is adenosine.

70. (Withdrawn) The use of a glutaminergic agonist for the manufacture of a medicament for modulating the body weight of a mammal.

71. (Withdrawn) The use of claim 70 wherein the glutaminergic agonist is glutamate.



72. (Withdrawn) The uses according to any one of claims 57, 58, 65, or 66 further comprising the use of leptin for the manufacture of said medicament for modulating the body weight of a mammal.

73. (Withdrawn) The use according to claim 72 wherein said leptin is selected from the group consisting of leptin comprising the amino acid sequence set out as SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, consensus leptins, variants, analogs, leptin fusion proteins, chemically modified derivatives of leptin, and fragments thereof, said leptin optionally having an N-terminal methionine.

74. (Withdrawn) The use of any one of claims 57, 58, 65, 66, or 72 wherein modulating body weight is reducing body weight.

75. (Withdrawn) The use according to claim 72 wherein modulating body weight is reducing body weight.

76. (Withdrawn) The use of any one of claims 57, 59, 60, 68, 69, 70, or 71 wherein modulating body weight is increasing body weight.

77. (Cancelled)